REMARKS/ARGUMENTS

Claims 1 and 3 have been revised to include the features of glutamic acid or glutamine at residue 250 in combination with leucine or phenylalanine at residue 428.

Claims 1 and 3 have also been revised to reference the variable region of daclizumab. No change in claim scope is intended or believed to have occurred.

Claim 5 has been revised to be in independent form.

The above described revisions to the claims are all consistent with the election in response to Restriction and requirement for election of species. They do not reflect any acquiescence to any rejection of record and are not made for any reason related to patentability. Applicants expressly reserve the right to pursue the subject matter of the claims, prior to the revisions, in a continuing application.

Information Disclosure Statement (IDS)

Enclosed herewith are forms PTO/SB/08A and PTO/SB/08B provided as a Supplemental IDS. Copies of the documents AT, AU and BA-BH in compliance with the requirements of 37 CFR §1.98(a)(2) are enclosed. A copy of document AV was previously provided with copies of other documents and form PTO-1449 via an Information Disclosure Statement mailed October 28, 2004. Unfortunately, that earlier filed form PTO-1449 contained an error in the indicated publication date for document AV. The inclusion of the correct information in the current IDS is provided in the interest of compliance with 37 C.F.R. §1.98(b)(4).

The earlier filed form PTO-1449 also included a number of documents among AA to AM which were cited without compliance with 37 C.F.R. §1.98(b)(4). Therefore, Applicants have included them in the instant form PTO/SB/08A to provide compliance with 37 C.F.R. §1.98(b)(4).

It is respectfully requested that the cited documents be expressly considered during the prosecution of this application, and the documents be made of record therein and appear among the "references cited" on any patent to issue therefrom.

Interview Summary

Applicants thank Examiners Crowder and Gambel for the courtesy of a telephonic interview with the undersigned on October 10, 2006. During the interview, the undersigned pointed out the disclosure and guidance provided by the instant application with respect to the elected invention, comprising substitutions at positions 250 and 428 of the heavy chain constant region. Examples of the disclosure include Figures 11A and 11C as well as content in Example 6 of the application.

Additionally, the undersigned pointed out the more than additive effects observed with combinations of substitutions as shown in Tables 3-8 in Example 6. The undersigned then pointed out how the Martin et al. document does not disclose or suggest the particular substitutions or the greater than additive effect seen with their combination. Because the particular substitutions were not disclosed or suggested, the combination of Martin et al. with the Hinton et al. document was improper, as indicated by a review of subject matter like that of claim 5, which was included in the alleged rejection based on anticipation. Examiner Gambel generally agreed with respect to residue 250.

Upon further review of the Action, the Examiners also indicated that there was an error in the Action in that the rejection under 35 U.S.C. § 112, second paragraph, should have been under 35 U.S.C. § 112, first paragraph. The undersigned indicated his surprise and confusion at the Examiners' comments because the statement of the rejection was wholly consistent with a rejection under 35 U.S.C. § 112, second paragraph. The undersigned indicated that Applicants would take this information under advisement.

Restriction Requirement/Elected Invention

While Applicants confirm the previous election of subject matter for examination, Applicants point out that in addition to the error in not presenting a rejection under 35 U.S.C. § 112, first paragraph, there was an improper withdrawal of claim 29 from consideration.

Briefly, Applicants confirm the election of the species of

(1) Daclizumab as the unmodified antibody.

(2) Positions 250 and 428, EU numbering, as a specific set of positions.

(3) Glutamine and leucine as the specific substitutions.

As previously pointed out, the sequences of certain heavy chains of modified daclizumab are SEQ ID NOS. 119-128. The daclizumab light chain is SEQ ID NO:118. SEQ ID NOS. 122 and 127 are IgG1 and IgG2 isotypes, respectively, of daclizumab in which positions 250 and 428, EU numbering, are occupied by glutamine and leucine respectively (see positions 249 and 427 in SEQ ID NO:122 and positions 245 and 423 in SEQ ID NO: 127).

In light of the above, Applicants were surprised by the indication of claim 29 as withdrawn from consideration, because claim 29 is also directed to the elected species of an antibody with residues 250 and 428, EU numbering, of the heavy chain constant region substituted by glutamine and leucine, respectively. As such, claim 29 and examined claim 28 are very similar in scope, with SEQ ID NO:127 in claim 29 being representative of daclizumab with a modified gamma-2M3 heavy chain and SEQ ID NO:122 in claim 28 being representative of daclizumab with a modified gamma-1 heavy chain.

Accordingly, Applicants respectfully submit that the failure to examine claim 29 was in error and that consideration of claim 29 should occur.

Alleged Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1-8, 13, and 38-41 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of "daclizumab".

As noted above, Examiners Crowder and Gambel indicated during the telephonic interview of October 10, 2006 that this rejection was in error and that a rejection under 35 U.S.C. § 112, first paragraph, was intended.

While Applicants respectfully submit that the statement of the instant rejection appears internally consistent and so contains no indication of a rejection under any other statutory provision, Applicants understand the Examiners' position to be that no rejection under 35 U.S.C. § 112, second paragraph was intended and so this rejection is effectively withdrawn.

Alleged Rejection Under 35 U.S.C. § 103

Claims 1-8, 13, 16, 28 and 38-41 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Queen et al., in view of Martin et al. and Krueger et al. Applicants have carefully reviewed the statement of the rejection and respectfully traverse because no *prima facie* case of obviousness is present.

The instant rejection appears to rely heavily upon the Martin et al. document. But none of Martin et al., Queen et al., or Krueger et al., alone or in any combination, discloses or suggests all of the features of the claimed subject matter as required to establish a *prima facie* case of obviousness (see the standard set forth at MPEP 2143.03 and the decisions cited therein).

More specifically, and as discussed during the telephonic interview on October 10, 2006, the Martin et al. document does not disclose or suggest i) the substitutions of glutamic acid or glutamine at residue 250, and does not disclose or suggest ii) a combination of these alternative substitutions at residue 250 and leucine or phenylalanine at residue 428, of the heavy chain constant region in an antibody.

With respect to the first of these deficiencies, Applicants point out that establishment of a *prima facie* case of obviousness against the subject matter in the rejected claims is not possible because each of the claims features specific substitution with either glutamic acid or glutamine at residue 250. So in the absence of a teaching or disclosure of these specific substitutions, the requirement for disclosing or suggesting all features of the claimed subject matter is not met.

Furthermore, the Martin et al. do not disclose or suggest the combination of specific substitutions at residues 250 and 428 as featured in many of the rejected claims. Stated differently, it is quite clear that Martin et al. do not disclose or suggest the substitutions of glutamic acid or glutamine at residue 250 and leucine or phenylalanine at residue 428 of the heavy chain constant region in an antibody. This failure to disclose or suggest the features of the claimed subject matter again prevents establishment of a *prima facie* case.

Additionally, Martin et al. also do not disclose or suggest that a combination of substitutions at residues 250 and 428, as featured in claims 1 and 3 for example, in a single molecule would result in more than additive effects in comparison to individual substitutions at the two residues. This is shown in at least Tables 3-5 of Example 6 in the instant application. For example, Table 3 shows that the relative binding of the T250E and M428F antibodies to be 3.5 and 3.2, respectively. But the combination of the two modifications results in an unexpected relative binding value of 15. Similar results are shown in Tables 4 and 5.

In light of the foregoing, Applicants respectfully submit that no *prima facie* case of obviousness is present, and so this rejection may be properly withdrawn.

Alleged Rejections Based on Obviousness-Type Double Patenting

Claims 1-8, 13, 16, 28, and 38-41 were provisionally rejected as unpatentable over claims 1-5, 8-12, 19-21, 25-28, 34-43, and 49 of commonly assigned, copending application 10/687,118; claims 1-4, 14, and 15 of commonly assigned, copending application 11/102,621; and claims 1-8, 13, 15 and 16 of commonly assigned, copending application 10/966,673. The statement of the rejection points out that a Terminal Disclaimer may be used to obviate this provisional rejection.

Applicants request that these provisional rejections be held in abeyance until the claims are otherwise allowable and the issue of obviousness-type double patenting is held as remaining.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6100.

Respectfully submitted,

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